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EXAMINER

GILLESPIE, BENJAMIN

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/533,041
Filing Date: December 14, 2005
Appellant(s): ROBY, MARK

Michael R. Brew
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 12/16/2008 appealing from the Office action mailed 6/17/2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

4,804,691	ENGLISH ET AL	02-1989
6,339,130	BENNETT ET AL	01-2002
4,057,535	LIPATOVA ET AL	11-1977
4,388,245	UEYANAGI ET AL	06-1983

(9) Grounds of Rejection

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The following ground(s) of rejection are applicable to the appealed claims:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Issue A - Rejection of claims 1-6, 8-9, 15-18, 20-22, and 24 under 35 U.S.C. 103(a) as being unpatentable over English et al ('691)

Claims 1-6, 8-9, 15-18, 20-22, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over English et al ('691). English et al teach a bioabsorbable tissue adhesive comprising polyester and aromatic diisocyanates, with the polyester backbone preferably derived from lactide, glycolide, and ϵ -caprolactone and initiated by 1,1,1-tris (hydroxy-methyl)ethane or ethylene glycol (Col 2 lines 60-68; col 3 lines 1-19). In particular patentees explain that the aromatic diisocyanate is present in excess by as much as a 6:1 NCO:OH ratio (Col 7 lines 63-65). Therefore, although not explicitly stated the reaction system contains isocyanate-terminated prepolymers but also additional diisocyanate monomer.

Although English et al teach that the bio-absorbable polyesters may be based on di or tri functional compounds, patentees fail to teach a polyurethane system that is a mixture of both. Nevertheless it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. *In re Kerkhoven* 205 USPQ 1069.

Issue B - Rejection of Claim 23 under 35 U.S.C. 103(a) as being unpatentable over English et al ('691) in view of Bennett et al ('130)

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over English et al ('691) in view of Bennett et al ('130). Aforementioned, English et al teach a polyurethane adhesive comprising the reaction product of isocyanate-terminated bio-absorbable polyester prepolymers, and important to note is that English et al further teach said adhesive may contain catalyst such as 1,4-diazabicyclo [2,2,2] octane, however there is no disclosure correspond to appellants' cure time of claim 23 (Abstract).

Bennett et al teach an adhesive comprising a (A) bio-absorbable oligomeric ester, (B) tri-functional compound, and (C) diisocyanate, wherein (A) and (B) are terminated with isocyanate groups (Abstract; col 3 lines 39-57; col 4 lines 37-60; col 5 lines 58-67). Important to note is that Bennett et al teach the adhesive composition is cross-linked through the aid of 1,4-diazabicyclo[2.2.2]octane, at a temperature between 20°C and 40°C, and as little as five minutes (Col 6 lines 22-37).

Although Bennett et al specifies that the selection of diisocyanate is important and certain aromatic diisocyanate should not be employed because of toxicity concerns, it still would have been obvious to utilize the cross-linking parameters of Bennett et al in the composition of English et al based on the motivation that Bennett et al do not limit certain diisocyanates, and the composition of English et al has been clearly disclosed for use as a living tissue adhesive and therefore is safe for in-situ applications. Another important note is that the both teach 1,4-diazabicyclo[2.2.2]octane as the cure catalyst, wherein the curing takes place in at the same

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temperatures, and the reactive species present during cross-linking, i.e. isocyanate groups and water, are the same.

Issue C - Rejection of Claims 1-9, 13-22, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipatova et al ('535) in view of English et al ('691) and Ueyanagi et al ('245)

Claims 1-9, 13-22, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipatova et al ('535) in view of English et al ('691) and Ueyanagi et al ('245). Lipatova et al teach a tissue adhesive composition comprising bioabsorbable compounds that are end-capped with aromatic diisocyanate, and aromatic diisocyanate (Col 1 lines 33-48, 66-67). Specifically, patentees explain the aromatic diisocyanate consist of 4,4'-diphenylmethane diisocyanate, naphthalene diisocyanate, and toluene diisocyanate (Col 2 lines 20-23).

Lipatova et al also teach a method of adhering a first and second tissue together via said composition, sealing a defect in tissue via said composition, wherein the seal prevents leakage of bodily fluids, and the composition is cross-linked through contact with water (Col 1 lines 24-26; col 4 lines 58-68; and col 9 lines 3-6). Still, patentees fail to teach bioabsorbable polyester that corresponds to appellants' claims and trifunctional adducts of the aromatic polyisocyanate.

Aforementioned, English et al teach bioabsorbable tissue adhesives comprising polyester and aromatic diisocyanates, with the polyester backbone preferably derived from lactide, glycolide, and ϵ -caprolactone and initiated by pentaerythritol or ethylene glycol (Col 2 lines 60-68; col 3 lines 1-19). Patentees go on to explain that these polymers have the advantage of

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acting as normal constituents in metabolic pathways after being broken down by hydrolysis, and therefore are less toxic to the user (Col 2 lines 18-22).

Therefore it would have been obvious to one of ordinary skill in the art at the time of invention to utilize the polyesters of English et al in Lipatova et al based on the motivation that both teach bioabsorbable tissue adhesives based on polyester backbones and aromatic diisocyanates, and the polyester of English et al is less toxic for the user.

Ueyannagi et al teach adhesives containing tri-isocyanate functional urethane adducts of diisocyanate, which are the reaction product of tri-functional alcohols such as trimethylolpropane or glycerin and aromatic diisocyanate (Abstract; col 1 lines 5-17; col 3 lines 17-25; col 7 lines 38-40, 46-47; col 8 lines 47-50). Specifically, patentees explain that monomeric diisocyanate exhibit high levels of toxicity as well as high viscosities that usually require the addition of organic solvent or heating in order to obtain a level of adequate mixing prior to application. The relied upon urethane adducts overcome both of these deficiencies since they exhibit low viscosities at room temperature and will not diffuse out of a reactive composition (Col 1 lines 19-68; col 2 lines 1-56).

Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to include tri-functional urethane adducts of aromatic diisocyanate as disclosed by Ueyannagi et al in Lipatova et al based on the motivation that both are drawn to polyurethane based adhesives, the urethane adduct allows for enhanced mixability and reduced toxicity, which is preferred in bio-applications, and it is prima facie obvious to add a known ingredient for its known function; *In re Linder* 173 USPQ 356; *In re Dial et al* 140 USPQ 244.

Finally regarding the amounts of claims 13 and 14, although Liptova et al teach the polyester based urethane prepolymer may be present between 30 and 99% by weight of total composition, there is no teaching to as how much the diisocyanate monomer and adduct should be present. Nevertheless it would have been obvious to arrive at appellants' claimed ranges based on the presence of the adduct has an effect on the resulting viscosity of the polyurethane reaction system, i.e. the amount is a result effective variable, and it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977); *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

(10) Response to Argument

Response to Issue A - Rejection of claims 1-6, 8-9, 15-18, 20-22, and 24 under 35 U.S.C.

103(a) as being unpatentable over English et al ('691)

Appellants argue the claimed invention has not been rendered obvious by the prior art because while English et al teach a compositions comprising

- (i) aromatic diisocyanate with
- (ii) an isocyanate end-capped compound

Component (ii) isocyanate end-capped compound of English et al is *either*:

- (iia) di-functional isocyanate-terminated bioabsorbable oligomeric compound

OR

- (iib) trifunctional isocyanate-terminated bioabsorbable oligomeric compound.

Thus English et al fail to teach a composition comprising three different components and instead only teach two-component systems. Moreover, appellants argue that the examiner has failed to establish a prima facie case of obviousness since no motivation has been provided as to why one would modify the two-component teachings of English et al into a three component system.

It should be noted that (iia) corresponds to the claimed “bioabsorbable oligomeric compound that is end-capped with an aromatic diisocyanate” and (iib) corresponds to the claimed “trifunctional compound that is end-capped with an aromatic diisocyanate”.

In response, appellants are reminded that the examiner has already conceded English et al fail to teach a composition comprising **both** (iia) and (iib). Instead the examiner has relied upon the rationale of *In re Kerkhoven* 205 USPQ 1069 that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose.

This is reflected by modifying English et al so that the compositions:

I: (i) aromatic diisocyanate with

(iia) di-functional isocyanate-terminated bioabsorbable oligomeric compound

OR

II: (i) aromatic diisocyanate with

(iib) trifunctional isocyanate-terminated bioabsorbable oligomeric compound.

Are combined, i.e. **I + II**, thereby arriving at the claimed composition:

(i) aromatic diisocyanate with

(iia) di-functional isocyanate-terminated bioabsorbable oligomeric compound

AND

(iib) trifunctional isocyanate-terminated bioabsorbable oligomeric compound.

Furthermore, appellants have repeatedly ignored this rational, and have yet to submit any data establishing criticality in the claimed three-component composition over the current prima facie case of obviousness.

Response to Issue B - Rejection of Claim 23 under 35 U.S.C. 103(a) as being unpatentable over English et al ('691) in view of Bennett et al ('130)

Appellants argue claim 23 has not been rendered obvious by the prior art because Bennett et al fail to provide a teaching or suggestion as to why one would be motivated to modify the system of English into a three-component system, however, appellants' remarks have been rendered moot in view of the **Response to Issue A** discussed above.

Issue C - Rejection of Claims 1-9, 13-22, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipatova et al ('535) in view of English et al ('691) and Uevanagi et al ('245)

Appellants argue the claimed invention is not rendered obvious by the prior art because Lipatova et al only teach :

- (i) monomeric diisocyanate
- (ii) isocyanate-capped bioabsorbable polyester, and
- (iii) 2,4,6-tris(dimethylaminomethyl)phenol

And there is no teaching or suggestion in Lipatova et al to further include a tri-functional isocyanate-capped compound. Moreover, English et al and Ueyanagi et al fail to rectify the deficiencies of Liptova et al because English et al and Ueyanagi et al also fail to teach a three component system comprising the claimed:

- (i) monomeric diisocyanate
- (ii) isocyanate-capped bioabsorbable oligomer, and
- (iii) tri-functional isocyanate-capped compound.

In response and as previously stated in the FINAL rejection mailed 6/17/2008, it is noted that each reference alone fails to teach the claimed composition – had any of the references disclosed the claimed composition the current application would be rejected under 35 U.S.C. 102 as being anticipated by Lipatova et al, English et al or Ueyanagi et al. Instead it is important to appreciate the prima facie case of obviousness based on the *combination* of references.

Specifically, Lipatova et al teach a composition comprising:

- (i) monomeric diisocyanate and
- (ii) isocyanate-capped bioabsorbable polyester

And on column 1 lines 66-68 and column 2 lines 1-7 of Lipatova et al teach that bio-compatible adhesives can exhibit problems with high toxicity level when *large* amounts of monomeric diisocyanate are used – said diisocyanate leaches out of the adhesive over time. Still Lipatova et al requires said monomeric diisocyanate since it improves the strength of the resulting adhesive.

With this understanding, appellants attention is directed back to Ueyanagi et al, which teach that the relied upon trifunctional urethane adduct is a useful alternative to using only large

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amounts of monomeric diisocyanate since said adduct can perform the same function as the monomeric diisocyanate while not leaching out over time.

Thus, while each reference *alone* does not teach or suggest the claimed composition, the *combination* of references does in fact suggest the claimed composition since one would be motivated to substitute at least some of the monomeric diisocyanate in Lipatova et al with the trifunctional adduct of Ueyanagi et al since it can reduce the amount of monomeric diisocyanate that may leach out overtime – thereby increasing the adhesive's bio-compatibility.

Finally, Lipatova et al teach in vivo applications, as the relied upon adhesive is applied in living rabbits and rats (Col 5 lines 12-15).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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Examiner, Art Unit 1796

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Supervisory Patent Examiner, Art Unit 1796

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